The Impact of Ozone

The wholesome, all-American images of summer—backyard barbecues, lazy Sunday picnics, raucous weekend baseball games, and grueling 10K runs beneath bright blue skies—are as familiar as fireworks on the Fourth of July. But in modern, industrialized America, another familiar summertime phenomenon is not so wholesome: the thick, white ozone-laden haze that shrouds areas throughout the country and can transform summertime activities, like jogging or bicycling, into unhealthy past-times, especially for children, asthmatics, and others with respiratory ailments.

Unlike the four other main air pollutants—carbon monoxide, sulfur dioxide, nitrogen dioxide, and particulates—for which the EPA has established National Ambient Air Quality Standards (NAAQS), ozone is not directly emitted into the air from automobiles, power plants, or industrial facilities. Instead, it is a photochemical pollutant, created when sunlight catalyzes chemical reactions with other pollutants.

The main culprits in ozone formation, called "ozone precursors," are nitrogen oxides, which are emitted from vehicles and power plants, and volatile organic compounds, which stem from numerous activities such as house painting, refueling of vehicles, and road paving. But controlling ozone precursors may not solve the ozone problem. A lot depends on the weather.

Setting Standards

Hot temperatures and stagnant air provide the right conditions for formation of ozone. During the hot summer of 1988, 112 million Americans were living in areas with ozone levels that exceeded, for at least one hour, the EPA's 0.12 parts per million (ppm) standard, compared to an estimated 42.6 million Americans who in 1992 lived in areas where ozone exceeded the standard. The Los Angeles metro area, where ozone levels have at times tripled the EPA standard, is the only locale nationwide that is classified in "extreme" nonattainment with the standard. Fewer than a dozen cities, including Houston, Chicago, and San Diego, qualify for the "severe" nonattainment designation.

The American Lung Association (ALA) estimated in 1991 that 151 million Americans lived in areas where ozone levels are unhealthy, including 31.6 million living in areas that meet the federal ozone standard, but have levels high enough to cause adverse health effects. Based on 1993 data, the EPA estimates that 51 million Americans live in areas where ozone levels exceed the EPA's standard.

The current ozone standard has been in existence since 1979, which prompted the ALA to sue the EPA in 1991 for failing to assess, and possibly revise, the standard every five years as required by the Clean Air Act. As part of the settlement of the suit, the EPA agreed to review the standard, but determined in 1993 that no revision was necessary. The ALA sued again, challenging the EPA's decision, citing recent studies indicating that adverse health effects such as reduced lung function, wheezing, coughing, shortness of breath, and chest irritation occur at levels below 0.12 ppm over an eight-hour period.

In 1994 the EPA announced it would review the ozone standard and possibly revise it by 1997. The year before, the EPA updated the ozone criteria document, a compilation of scientific information about ozone and its health effects which forms the basis for the ozone standard. In February 1995, EPA staff reviewed the criteria document and offered preliminary recommendations for revising the standard. The staff recommended an eight-hour standard of 0.07–0.09 ppm, either in addition to the current 0.12 ppm per one-hour standard, or by itself. Ozone concentrations would be averaged

Sunlight and shadows. Ozone is formed by reactions between sunlight and pollutants such as nitrogen oxides from auto emissions and volatile organic compounds from paint spraying.

over an eight-hour period and could not exceed the standard. The Clean Air Scientific Advisory Committee, an independent scientific body that advises the EPA on matters related to the Clean Air Act, approved the bulk of the criteria document, except the chapter on ecosystem effects, which the EPA is now reviewing.

The newest criteria document encompasses some major improvements in knowledge about ozone health effects that occurred since the document was last revised in 1986 (a supplement was released in 1992). Much more information is now available on exposures over a six- to eight-hour time frame, according to Judith Graham, associate director of the EPA's Environmental Criteria and Assessment Office.

The EPA's 1986 document included studies showing that ozone caused inflammation in the lungs of rats and rabbits, Graham said. Since then, human clinical studies have demonstrated inflammatory responses. More is also known about lower levels of exposure in animals. In animals, changes occur in the epithelium of the deep lung, the walls of the alveoli get thicker, and the cells that line the alveoli change. "These changes are consistent with what happens in a young cigarette smoker," said Graham. Although extrapolating from animal effects to humans is problematic, Graham noted, the animal data do "raise the concern about the potential of ozone to cause chronic effects."

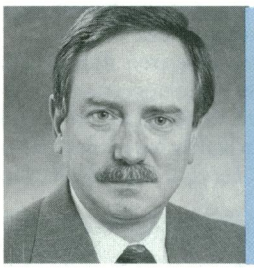
David McKee, the EPA's ozone NAAQS review program manager, also noted the improvement in information about long-term (eight hours or more) exposures and about chronic effects, such as lesions in the lungs in the region where air exchange occurs, as well as structural changes and changes in the elasticity of the lungs. These effects might suggest the potential for more breathing problems as individuals age, and possible early mortality, McKee commented.

McKee said an eight-hour standard might be more protective of human health in cities where hourly ozone concentrations may approach the 0.10–0.11 ppm level for six or seven hours out of a day, but never rise to the 0.12 ppm level, and therefore avoid exceeding the standard. Residents in those areas could be exposed to relatively high levels of ozone, which, based on laboratory studies, may cause significant health effects, even though the area would not be out of compliance with the standard.

Effects of Ozone

Ozone is a powerful irritant to the respiratory tract. It constricts the air passages, making breathing labored, particularly in young children and the elderly, and people with asthma, chronic bronchitis, or emphysema.

Ozone also is a "powerful cellular poison that interferes with the ability of the lung to defend itself against other offending agents," says Alfred Munzer, past president of the ALA and director of critical care and pulmonary medicine at the Washington Adventist Hospital in Takoma Park, Maryland. Ozone affects alveolar macrophages, which act as scavenger cells in the lung, engulfing harmful bacteria. By interfering with macrophages, ozone makes the lung more susceptible to infection. "This is why several days after a [smog] alert, we will see an increase in respiratory illness," says Munzer.



Ozone is a powerful cellular poison.

—ALFRED MUNZER

Washington Adventist Hospital

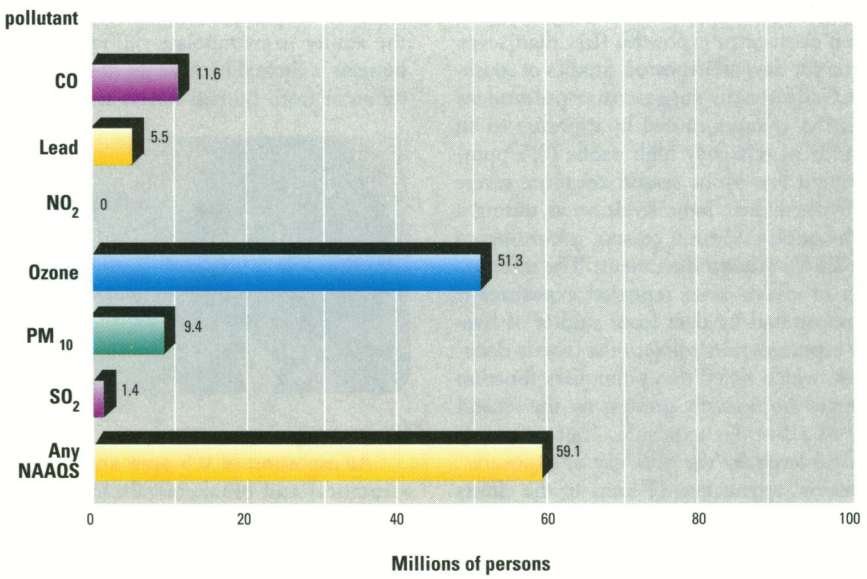
Ozone's effects are not limited to especially sensitive individuals. "Even in healthy individuals, if they exercise vigorously outdoors, when the air pollution levels are high, their breathing rate goes up, and the depth of respiration goes up so much, they are exposed to considerable amounts [of ozone], and exhibit the same harmful effects" as those with respiratory problems, Munzer said.

Munzer also notes that recent hospital admissions studies demonstrated correlations between increased admissions and ozone levels, even at levels below the EPA's 0.12 ppm standard.

In April, the ALA reported that 27.1 million children live in areas where, on at least four occasions between 1991 and 1993, ozone concentrations exceeded 0.085 ppm over an eight-hour period. Munzer said these findings demonstrate the need for revising the standard.

A similar position was adopted by the Environmental Health Committee of the American Academy of Pediatrics, which said the 0.12 standard contains little or no "margin of safety" for children who play outdoors. In a report published in June 1993 in *Pediatrics*, the academy's journal, the committee said children are at greater risk than adults because a child's smaller airways will be more affected by irritation caused by ozone than an adult's and because children's oxygen needs are greater relative to their size. "They breathe more rapidly and inhale more pollutant per pound of body weight than do adults," the report said, and they often spend more time outdoors.

Philip Landrigan, director of the Mount Sinai Environmental Health Sciences Center and liaison for the academy's Environmental Health Committee, said studies of young teens attending summer camps in the Northeast found that the children experienced respiratory problems on days when air pollution levels were high. Pollution also plays a role in hospital admissions for asthma, which, he said, has become a leading reason for children to be hospitalized. "It's much worse than it used to be. The numbers have increased dramatically, and ozone is a potent



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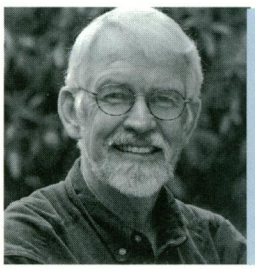
The air we breathe. The EPA estimated the number of people living in counties with air quality levels not meeting the primary NAAQS in 1993.

cause of asthma, all by itself," Landrigan said, but the effects are worsened when ozone is combined with other pollutants.

Recent hospital admissions data have helped clarify the relationship between ozone and health effects, according to George Thurston, associate professor at the Nelson Institute of Environmental Medicine of the New York University School of Medicine. "There's been a spate of new studies that have shown a very strong association between summertime ozone levels and increased respiratory hospital admissions," he says.



There is some evidence of ozone's carcinogenicity.

—GARY BOORMAN

NIEHS

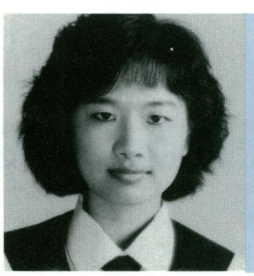
Hospital admissions data, including summertime studies in Toronto, New York City, and Buffalo, New York, demonstrate that individuals with respiratory ailments end up in the hospital more frequently during the ozone season, even when ozone levels do not exceed the standard, according to Thurston. Individuals with compromised respiratory health are acting as the proverbial canary in the coal mine—warning the healthy population that ozone pollution is at unhealthy levels, he commented. Healthy individuals are also affected, but their symptoms or effects are not severe enough to require a visit to the doctor.

Getting Used to It

Visits to the doctor or hospital during high-ozone days might also be limited by the body's "attenuation" or lessening of effects when short-term exposures (less than seven hours per day) are repeated. Studies of southern Californians suggest that pulmonary function changes caused by exposure to an episode of relatively high ozone (0.5 ppm) during a low-ozone season are more severe than when these same levels occur during a high-ozone pollution season, according to the EPA's criteria document. The attenuation of effects after repeated exposures is demonstrated by data from studies of five-day exposures, according to the criteria document, which noted that pulmonary function changes are typically greatest on the second day of a five-day exposure, "but return to control levels by the fifth day of exposure." However, attenuation of some of the effects reverses when exposure ceases and cell damage continues while the attenuation process is underway. Moreover, "attenuation may alter the normal distribution of ozone within the lung, allowing more ozone to reach sensitive regions, possibly affecting normal lung defenses," the document states.

For this reason, Thurston doubts that individuals who do not demonstrate symptoms when exposed to ozone are unharmed by it, or that their bodies have developed a tolerance. In fact, he said, individuals who do not experience effects may be at greater risk than those who experience difficulty breathing, chest tightening, or other effects. The effects are the body's defense mechanisms at work, attempting to keep ozone at bay. Individuals without those responses are welcoming more ozone into their bodies, "oxidizing and adversely affecting the lungs," Thurston said.

A recent animal study suggests that rats develop a tolerance to long-term (eight hours/day) ozone exposures. In that study, conducted by the National Toxicology Program in collaboration with the Health Effects Institute (HEI), healthy, sedentary rats were exposed to three different concentrations of ozone (0.12 ppm, 0.5 ppm, and 1.0 ppm) for 5 days a week, 6 hours a day, for 20 months. According to Daniel Greenbaum, president of HEI, the rats experienced relatively few health effects in the lung and other parts of the respiratory system, with the exception of the nose, where inflammation occurred at exposures of 0.05 ppm and 1.0 ppm. Although the inflammation was a type that could occur in humans, the ability to extrapolate the rat effects to humans is limited because rat noses are quite different from human noses, and are more likely to trap ozone.



Improved monitoring is the key to accurately assessing health effects.

—L.-J. SALLY LIU

U. of South Carolina

At exposures of 0.5 ppm and 1.0 ppm, structural and biochemical changes were found in certain regions of the lung, especially the centriacinar region at the beginning of the air exchange system. Data on the effects of 0.12 ppm ozone were inconclusive. Ozone causes damage and death of epithelial cells, accompanied by inflammation at the end of the airway, which interferes with the body's ability to carry particles out of the lung. These effects were apparent in the rats exposed for 20 months under the HEI study, but the effects were similar to those exhibited by rats in other studies that were exposed for 90 days, suggesting that past a certain point, additional exposure may not produce additional harm.

"The investigators felt these changes suggested that rats became tolerant to the effects of ozone," said Greenbaum. However, Greenbaum noted that the committee reviewing the study was not certain it demonstrated tolerance. "Our review committee didn't necessarily reject it out of hand, but because the experiment wasn't designed to test tolerance, they were more hesitant to say [the results demonstrated] tolerance."

In comparing the results of rat studies to human effects, the committee said the effects experienced by the rats were not similar to the more serious human pulmonary fibrosis, or scarring of lung tissue, but instead resembled bronchiolitis, or inflammation of the bronchioles, the small branches that extend from the bronchial tree, a condition that produces limited or no functional impacts.

Ozone and Cancer

The NTP's evaluation of the potential long-term toxicity of ozone also included work on the chemical's carcinogenicity, a topic about which there is limited information. No conclusive evidence exists to link ozone exposure to lung cancer in humans, according to the NTP's work. Three of four animal studies conducted between 1985 and 1993 that are cited by the NTP revealed no increase in lung neoplasms from ozone exposure, and the findings about ozone's promotion effects were unclear.

In one NTP study, investigators exposed approximately 2,000 rats and mice to 0.12, 0.5, and 1.0 ppm of ozone, five days a week, for six hours a day, over two years. Rats were also exposed to ozone in combination with a lung carcinogen, 4-(*N*-methyl-*N*-nitrosamino)-1-(3-pyridyl)-1-butanone, or NNK, which is found in tobacco smoke. "Lifetime" studies were conducted for 30 months at concentrations of 0.5 and 1.0 ppm of ozone, without NNK.

The rat data provided no evidence that

ozone alone could initiate or enhance spontaneous incidence of cancer or would further promote cancer in the NNK-exposed rats, according to NIEHS researcher Gary Boorman. The study, he noted, was designed to enhance the probability that a cancer relationship would be demonstrated by selecting a carcinogen (NNK) that affects the same cells as ozone. "The lack of an effect would suggest that with this chemical, ozone has no promoting effect at all in rats," Boorman said.

The mouse data, however, demonstrated a marginal increase in lung tumors in male mice and a more pronounced effect in female mice for both the two-year and lifetime studies. "The female mice effect was more dramatic," he said. "We considered it to be some evidence of carcinogenicity."

The conflicting data "make it difficult for policy-makers," Boorman observed, and "the question becomes which animal is predictive [of human effects]." The mouse findings could be due to chance, or to physiological differences between mice and rats. Mice have a higher incidence of lung tumors, and mice may be less resistant to the induction of lung tumors than rats.

NIEHS researchers discovered genetic alterations in the lung tumors of the ozone-exposed mice that have not been seen in other studies. This work, according to researcher Robert Sills, is the first study of genetic alterations in ozone-induced tumors. The genetic mutations found in the tumors from the ozone-exposed mice were different from the spontaneous tumors that appeared in the nonexposed mice. The molecular data demonstrate that some of the DNA damage is consistent with ozone exposure and that ozone is probably influencing the carcinogenic process in mice, Sills said.

HEI's Greenbaum believes more work is needed to determine whether animals develop tolerance to ozone by examining lung function at various intervals of exposure. Evidence demonstrates that lung function is impaired after exposure to ozone, but "it's unclear whether a week after exposure that lung function is permanently impaired," Greenbaum said. Animal studies are also needed, he said, to determine at what intervals effects are experienced, which would provide a better understanding of how the effects develop.

Ozone Questions

Like other researchers, Greenbaum cited the need to understand more about the effects of ozone in combination with other pollutants, noting the difficulty of replicating real world air pollution in a lab. For this reason, research focusing on effects of a combination of pollutants will initially center on epidemiology studies, he commented.

One such study, the Harvard Six Cities Study, examined morbidity and mortality by following 8,842 adults and 14,357 children in Steubenville, Ohio; St. Louis, Missouri; Kingston and Harriman, Tennessee; Watertown, Massachusetts; Portage, Wisconsin; and Topeka, Kansas. The study began in 1974, and data from the study are continuing to be analyzed, according to Douglas Dockery, one of the principal researchers and a professor at the Harvard School of Public Health. Although the study was designed to assess the impacts of fine particles, which are the decay products of sulfur oxides and, like ozone, are photochemically produced, results may yield information about ozone as well.

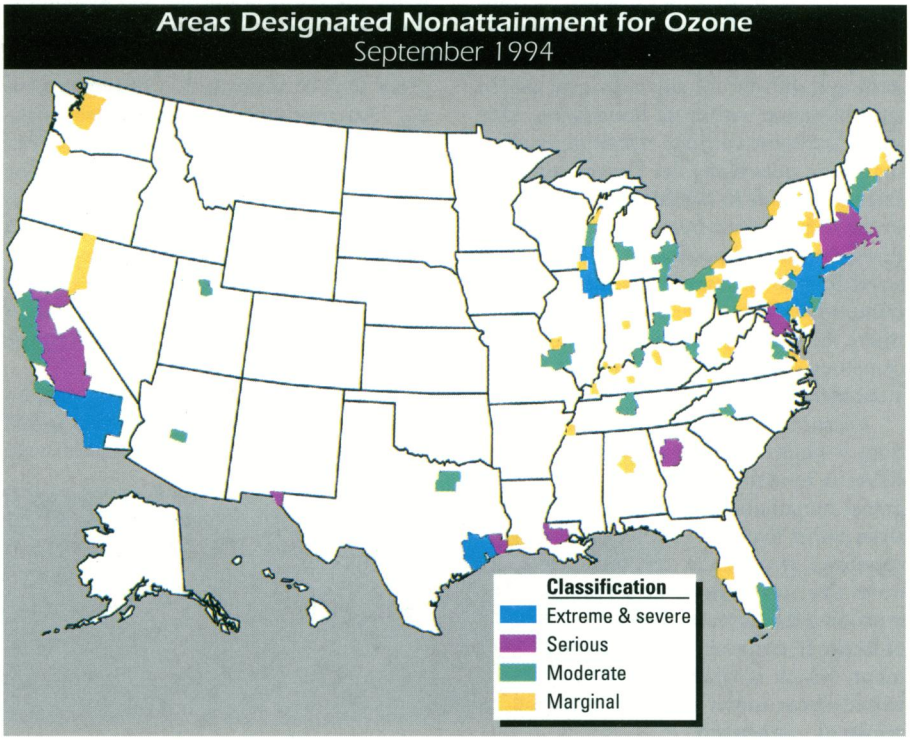
The study showed that when ozone concentrations climbed, so did other pollutants (although not necessarily in proportion). Although both ozone and fine particles cause health effects, the effects are separable, Dockery said. Both produce inflammatory responses and decreased lung function, but there are differences in how people react to the two pollutants. Ozone produces immediate reactions, whereas effects of particle exposure may not be noticeable until several days after the exposure.

Some effects in the study appeared to be more closely related to fine particle concentrations than to ozone, Dockery said. In some cities, pulmonary function effects were demonstrated where there was particle exposure, but no ozone. Dockery added, "I'm not trying to suggest that health effects are all due to particles, but there are at least two actors—particles and ozone—and possibly more."

Among the challenges facing epidemiologists is accurately gauging exposure levels. L.-J. Sally Liu, assistant professor in the University of South Carolina's environmental health science department, believes improved monitoring is key to accurately assessing health effects. By using badge-type monitors worn by participants, Liu studied the personal exposures of individuals living in State College, Pennsylvania, to correlate individual exposures with readings at central monitoring stations. "We found that personal exposures were very different than what was measured at the central monitors," she said. For this reason, studies that rely on central monitoring stations to gauge individual exposure may produce inaccurate conclusions about whether ozone caused certain effects, she said.

Accurately assessing an area's ozone problem is quite a challenge. Because of the role weather plays, the EPA examines three years of data to determine whether an area should be classified as "nonattainment" for the ozone standard. The influence of weather also explains why the number of nonattainment areas has dropped by around 10% from last year's total of 92.

Daniel Mussatti, an economist with the innovative strategies and economics group of the EPA's Air Quality Management Division, said some areas removed from the nonattainment list are "marginal" nonattainment areas where the emissions problem is not so great, but where weather conditions may have resulted in nonattainment status. Efforts to reduce emissions are also contributing to the declining number of nonattainment areas.



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Ozone control, Mussatti noted, is complicated by the fact that the pollutant is transported across entire regions by wind, making it difficult for any individual area to control ozone within its boundaries. One ozone transport corridor encompasses all of the major cities along the Eastern seaboard, extending south to Washington, DC, north to the U.S.–Canada border, west to western Pennsylvania, and possibly as far as Chicago, according to Mussatti. Because ozone is transported, "there are areas of the country where they could shutdown everything [that contributes to ozone] and still not achieve attainment."

Given the regional nature of ozone pollution, it might be more appropriate for the EPA to identify regional nonattainment areas, rather than metropolitan areas, as is now the case. But expanding the number of locales in nonattainment, which is what would occur under a regional approach, would be politically unpopular, Mussatti noted. The stigma associated with nonattainment status and the fact that nonattainment areas cannot add new pollution sources without identifying offsetting reductions lead communities to fear the nonattainment label, said Mussatti. "We wind up with small postage stamps of nonattainment areas, when the problem is more like the size of an envelope."

EPA

A regional approach to ozone control might be more effective, though unpopular.

—DANIEL MUSSATTI

Communities trying to meet the ozone standard face considerable difficulties stemming from the nature of the standard and the limitations of computer models designed to predict ozone violations, according to Harvey Jeffries, professor of atmospheric sciences at the University of North Carolina at Chapel Hill.

The models are supposed to accurately predict when a violation will occur by analyzing the effects of weather and monitoring data and information about ozone precursor sources that is drawn from a handful of high-ozone days occurring over a three-year period. "Attempting to simulate those [high-ozone] days is an incredible task," Jeffries commented. Even if the model simulates one "base case" event, it may not accurately predict another event when new data about weather, sources, or monitoring are plugged into the model. Moreover, failing to keep pace with all of the changes affecting sources and emissions control will hinder the model's accuracy.

Jeffries also believes that using data on high-pollution days from a three-year period overstates the impact of weather, since cyclic changes may last longer than three years. Examining a community's track record over five years might decrease the "enormous role" that weather can play in pushing communities into nonattainment, he said.

The EPA's consideration of an eight-hour standard might also have a beneficial effect. For one, it would make it easier to model pollution events. Currently, models must predict where and when the standard will be exceeded for one hour, which is more difficult than predicting exceedences over an eight-hour period, Jeffries said. However, lowering the acceptable concentration to 0.08 ppm over the eight-hour period would make compliance tougher. "It's not hard to get to 80 or 90 [parts per billion]," he said; most of the eastern cities "constantly exhibit levels of 60 to 70 ppb."

A similar point was made by Theresa Pugh, senior regulatory analyst with the American Petroleum Institute. "If EPA were to go to an eight-hour standard [at 0.08 ppm], there would be 218 nonattainment areas," she said; "All industries would be impacted, not just the oil industry, but manufacturers of every type." API is in the early stages of developing a study to more precisely assess the socioeconomic impact of a 0.08 ppm eight-hour standard. Pugh noted that the kinds of controls that might be necessary, such as highway tolls, mandatory ride sharing, employer carpooling programs, and four-day work weeks, can be quite expensive. The impacts, she said, will not fall exclusively on businesses, but will produce "societal impacts we will all feel."

Ultimately, the EPA administrator will face the unenviable task of setting the ozone standard, but science should not be expected to provide clear-cut answers to setting a specific standard, says Boorman. "As the body of knowledge is built up, we get a better understanding of what chemical exposures mean and what is uncertain about the risk," he said. "Even today, we don't know what causes cancer, we don't know the exact mechanism of cancer initiation, so it's very difficult to exactly understand the chemical risk for cancer. That doesn't mean it is not important to study and to try to understand, but for the public and the policy-maker, its too much to expect a simple yes or no answer."

Karen Breslin